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## Gut microbiota and metagenomic diversity in Clinical Isolated Syndrome

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(Article begins on next page)

## Abstract

**Objective:** To investigate whether alteration in the composition of the gut microbiota, in terms of species richness, distribution and functional potential, could be associated with immune system alteration in Clinically Isolated Syndrome (CIS), as it offers the opportunity to study disease processes in the supposed earliest stage of Multiple Sclerosis (MS).

**Background:** Which are the triggers that convert self-reactive lymphocytes, normal components of the immune repertoire, into an autoaggressive phenotype facilitating the first episode of demyelization in MS are still poorly understood. Alterations in the composition of the gut microbiota are now suggested as having a role in the etiology, course and treatment of MS through gut-brain communications that likely involve the immune system.

**Design/Methods:** Stool and blood samples were collected from CIS patients and Healthy Volunteers (HV). DNA isolated from stools were subjected to shotgun metagenomic sequencing strategy in order to discover the microbiota composition as well as the microbial function. T helper (Th)17 and T regulatory (Treg) cells were analyzed by FACS in the peripheral blood (PB).

**Results:** A clear separation of the microbiota composition of CIS patients compared to HV was observed by using Principal Component Analysis. Two of the identified taxa driving cluster separation and decreased in CIS microbiota belong to butyrate-producing bacteria. In the PB, CIS patients displayed an increase of pathogenic Th17 cells expressing Toll Like Receptor 2 and a decrease of Treg cells producing Interleukin-10 and expressing CD39 compared to HV, evidences that could be indicative of gut microbial modulation.

**Conclusions:** These findings indicate that gut microbial dysbiosis exist at the onset of MS and could be suggestive of the pro-inflammatory milieu observed in the periphery. The analysis on metagenomic content and microbial gene identification will allow us to design strategies to modulate the immune system through alteration of gut microbiome.

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